Retinal artery obstruction, migraine and patent foramen ovale

It is well known that migraine is associated with both stroke and retinal artery obstruction, and evolving literature suggests that both migraine and embolic stroke may be due to paradoxical embolism from a patent foramen ovale (PFO).[1–3] We present a 24-year-old man with localised retinal artery obstruction, migraine with aura, and PFO. Early diagnosis and treatment of these cases may decrease the risk of future embolic events and stroke as well as helping with migraine symptoms.

Case report

A 24-year-old Caucasian man presented with sudden-onset painless scotoma in the right eye. We found no preceding aura, headache or nausea and he was otherwise well. He had a history of migraine with visual auras from the age of 16 years. His mother also had migraine. There was no other ocular, medical or family history. He was not on any drugs. He was systemically well, denied any previous drug use and was a non-smoker.

Visual acuities were 6/5 unaided in both the eyes. Pupillary reactions were normal, with no relative afferent pupillary defect. Visual fields showed a small right superior paracentral scotoma. Colour vision, anterior segments and intraocular pressures were all normal. Dilated funduscopy showed a large cotton-wool spot over the right inferior arcade, with an adjacent area of retinal pallor (fig 1). We found no associated vitritis, disc swelling, emboli, peripheral retinal abnormalities or haemorrhages. Left eye examination was unremarkable.

The patient showed no signs of jaundice, anaemia or lymphadenopathy. He was normotensive (blood pressure 120/75 mm Hg); his pulse was 70 beats/min and regular, with normal heart sounds. A chest and abdominal examination were unremarkable. There were no carotid bruits, and the remaining examination was normal with no focal neurological deficit.

Fluorescein angiography (fig 2) showed a masking of the choroidal background fluorescence corresponding to the cotton-wool spot. Filling of the retinal arteriole inferiorly was delayed compared with the superotemporal branch. No emboli, disc swelling or peripheral abnormalities were detected.

Investigations including full blood count, glucose, erythrocyte sedimentation rate, C reactive protein, serum electrophoresis, coagulation screen, blood cultures, autoimmune profile, chest *x*-ray, electrocardiogram and carotid Doppler ultrasound were all normal.

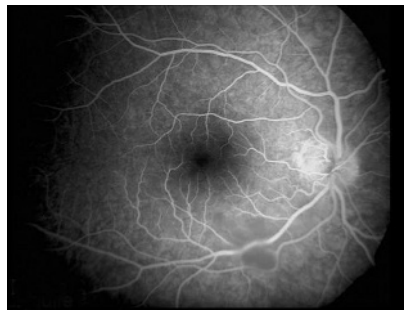

Figure 2 Fluorescein angiography of the right eye with masking of the choroidal background fluorescence corresponding to the cotton-wool spot.

A contrast echocardiogram showed spontaneous right to left shunting at the atrial level: a PFO. After discussion, this was closed by percutaneous closure under local anaesthesia with sedation, using a 20-mm helex septal occluder, with excellent results.

At the last follow-up, the patient was asymptomatic. The retinal changes resolved and he was free of migraines.

Comment

A PFO is a persistent interatrial communication. This usually closes spontaneously after birth; however, in 10–35% cases it remains patent throughout life.[4 5] In most people, its persistence does not cause any complications. However, several recent studies have shown a strong association between the presence of a PFO and the risk of embolism or stroke. The prevalence of PFO is fourfold higher in patients with stroke than in matched controls.[1] Migraine, especially with aura, has also been linked with PFO.[2 3 6] A randomised controlled study (Migraine Intervention with STARFlex Technology) detected PFO in 60.2% of patients with migraine (40% with large shunts), much higher than that expected in the normal population. Preliminary results showed that closure of PFO was associated with a 50% reduction in headache frequency compared with randomised controls.[6] Prior retrospective studies reported improvement in migraine in 62% of patients as a result of closure of the PFO.[2] Additionally, some atrial shunts may show a dominant inheritance associated with migraine with aura in some families.[3]

Although the association between migraine and retinal artery obstruction, noted by many, may be due to other mechanisms, we believe that patients with retinal artery obstruction and migraine, especially with aura, should be investigated for PFO. Early diagnosis and treatment of these cases may decrease the risk of future embolic events and stroke as well as helping with migraine symptoms.

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doi: 10.1136/bjo.2006.093617

Accepted 9 June 2006

Funding: No funding or previous presentation.

Competing interests: None.

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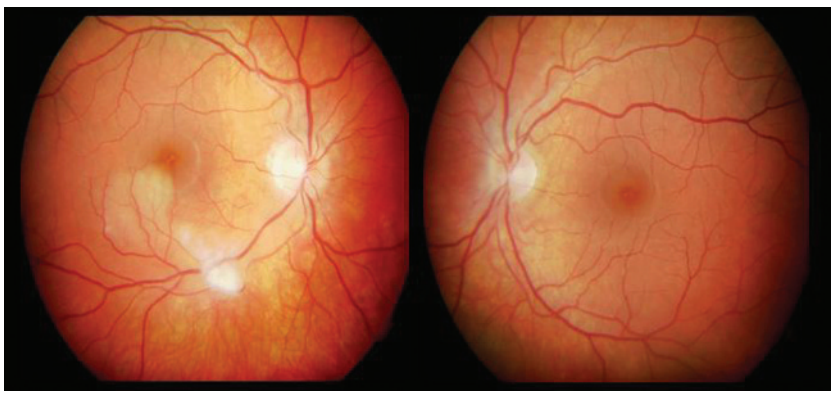

Figure 1 Colour fundus photographs show a large cotton-wool spot over the right inferior arcade, with an adjacent area of retinal pallor.

Diet-related mercury poisoning resulting in visual loss

A 36-year-old man with progressive peripheral neuropathies was referred to the eye clinic with failing visual acuity. No cause could be found for his ongoing weight loss, poor appetite, disturbed sleep and worsening painful neuropathies after extensive investigations. Blood tests identified a markedly raised mercury concentration, and further inquiries identified his diet to be rich in fish caught in the Caribbean. Tests carried out on the fish he provided showed a high concentration of mercury in the tissue. Electrophysiology showed changes consistent

Table 1 Visual electrophysiology

	Right eye	Left eye
Pattern VER P100	P = 103 ms N = 125 ms	P = 100 ms N = 126 ms
Pattern ERG P50	–	51 ms
Pattern ERG N95	–	90 ms

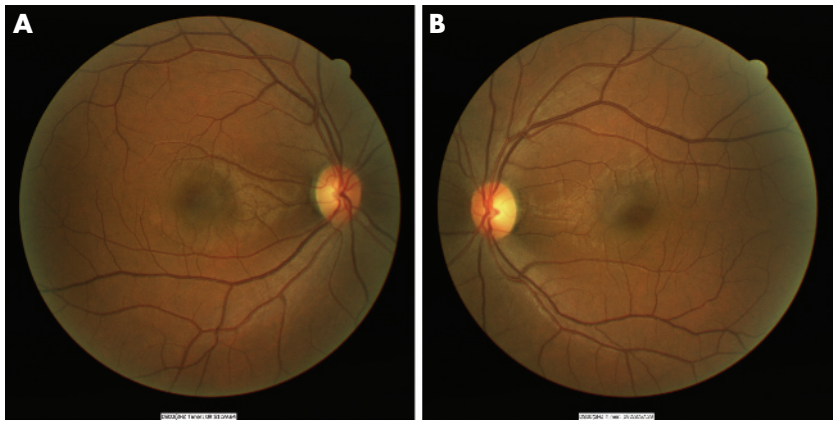

Figure 1 Maculae showing granular-type changes.

with published reports on patients regularly exposed to high levels of mercury.

A 36-year-old man was referred to the neuro-ophthalmology clinic with a 3-month history of deteriorating vision, with difficulty in reading. He was also being investigated by the neurology service for peripheral neuropathies. He had an 8-month history of numbness and tingling in both feet and in his fingertips. He had been generally unwell, with poor appetite, weight loss of one and a half stones, diarrhoea, low-energy levels and disturbed sleep. He smoked five cigarettes a day and denied any intravenous drug misuse.

He had no medical history or family history of note. There was no family history of consanguinity.

On examination, his best-corrected vision was 6/18 in the right eye and 6/24 in the left. Anterior segments were normal. He showed evidence of reduced colour vision on reading Ishihara colour plates, and had a normal optic disc appearance. Both his maculae showed granular-type changes (fig 1).

Muscle nerve biopsy and nerve conduction studies showed evidence of early sensorimotor neuropathy. On magnetic resonance imaging of the brain, no structural abnormality of the optic nerves, cerebrum or cerebellum was found. Humphry visual field analysis showed evidence of central field disturbance, with the right eye worse than the left (fig 2).

Extensive blood tests were carried out and normal levels of Vitamins A, B, C E, B_{12}, folate and ferritin were found. Serum acetanitrile, antinuclear antibodies and antineutrophil cytoplasmic antibodies were normal, as were blood glucose, liver function and thyroid function tests. Tests for an infectious cause (hepatitis screen, HIV, Veneral disease research laboratory) proved negative. Other tests included immunoglobulin electrophoresis, tests for C3 and C4 concentrations, chest radiography and lumbar puncture. All these results were normal.

We were surprised to find that the patient's blood mercury concentrations were raised at 68 nmol/l (equal to 13.9 µg/l). Further discussion with the patient about his diet identified his high intake of fish, especially the red snapper. This fish is known to contain high concentrations of mercury, and US Food and Drug Administration guidelines suggest that it should be consumed no more than once a month. Our patient was eating between 10 and 12 of these fish per week.

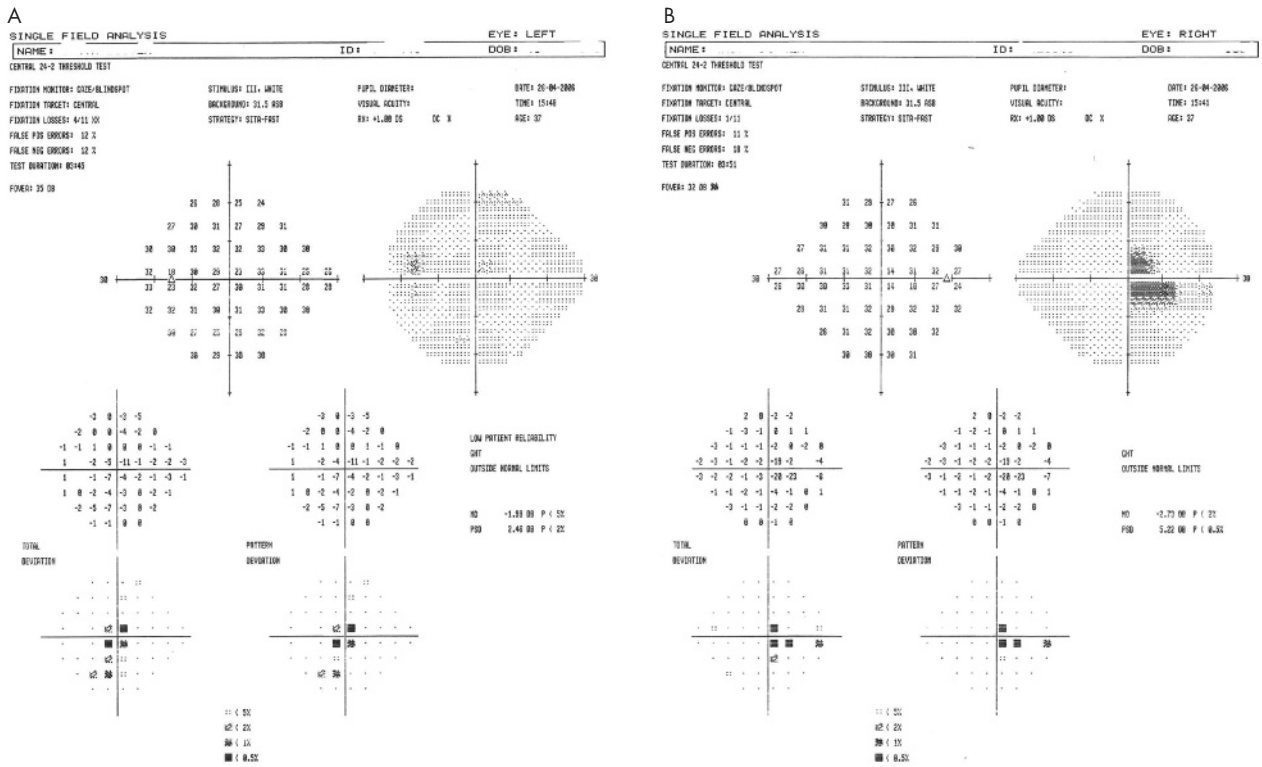

Figure 2 Single field analysis.

We tested two red snapper fish of the type he normally consumed and found tissue mercury concentrations of 0.47 and 0.66 μg/g. An average serving of fish is about 150 g. This suggests his average weekly mercury intake to be between 848 and 1017 μg. This is much higher than US FDA guidelines, which recommend that an average person should consume no more than 42 μg of mercury/week.

Electroretinography (ERG) carried out on our patient (table 1) indicates a bilateral optic neuropathy or bilateral cerebral visual pathway damage as the main cause of the reduced acuity. We also found diminished colour sensitivity, especially along the protan axis, as previously reported. These findings are reported as being ''consistent with damage to the optic nerves, and possibly the occipital cortex, as has been reported in mercury poisoning''. We believe that these results, combined with the patient's visual field abnormalities, suggest the primary cause of his visual loss to be bilateral optic neuropathies secondary to chronic mercury poisoning.

He consulted a dietitian for dietary advice and now avoids any likely source of mercury in his diet. In humans, about half the body burden of mercury can be eliminated in 70 days if no further mercury is ingested. We continue to monitor his progress in the neuro-ophthalmology clinic.

Discussion

Chronic mercury exposure in a large population was first studied following development of unexplained neurological symptoms in people living at Minamata Bay, Japan, in 1960 (giving it the name Minamata disease).

The most common source of mercury in our diet (in the form of methylmercury) is from the consumption of certain fish caught in known polluted waters. Tissue mercury concentrations increase in fish that have a longer lifespan, and larger predatory game fish (such as swordfish, shark and king mackerel) are likely to have the highest mercury concentrations.[1]

Exposure to methylmercury has been implicated in many conditions, including cardiovascular disease, peripheral neuropathies, psychiatric disorders and visual disturbance.[2] A ''safe'' blood mercury concentration for an adult male is uncertain. Our patient's blood mercury concentration was 68 nmol/l (13.9 μg/l). The US Environmental Protection Agency recommends keeping blood mercury concentration <5 μg/l. They found the mean blood mercury concentration among the US general population to be 1.3 μg/l.[3] A study conducted on a group of women from a Carribean island (Vieques) showed a median hair mercury concentration three times that of the US average.[4]

ERG carried out on our patient showed several abnormalities previously reported by Ventura *et al*[5] in patients with a history of mercury intoxication. We used the International Society for Clinical Electrophysiology of Vision protocol for multifocal ERG and pattern ERG as in the published study. Their paper noted that central retinal function was markedly depressed and in our patient, multifocal visual evoked potential showed almost abolition of the central responses in both eyes. Multifocal ERG in our patient also showed mild reduced amplitudes and delayed responses.

Neurological recovery after removal of the source of mercury is variable. Colour vision impairment as a result of occupational mercury exposure was noted to be reversible, with a return to normal after 12 months free from exposure.[6] Other symptoms such as peripheral neuropathies have been noted to persist with little improvement, even up to 30 years later, after prolonged occupational exposure to inorganic mercury.[7]

In these cases, an early diagnosis is important, as continued exposure could cause further mercury accumulation and more serious neurological damage. We are uncertain as to the likelihood of visual improvement and continue to monitor his progress.

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doi: 10.1136/bjo.2006.094821

Competing interests: None declared.

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Optical coherence tomography pseudo-macular hole appearance after photodynamic therapy

The case reports of two patients with myopia and one patient with age-related macular degeneration are presented. The patients were treated with photodynamic therapy for choroidal neovascularisation and have full-thickness retinal thinning in the area of treatment that mimics the appearance of a macular hole on optical coherence tomography (OCT). Ophthalmologists should recognise that this appearance does not represent a true macular hole when deciding how to manage these patients.

OCT distinguishes full-thickness macular holes (FTMH) from other entities such as lamellar holes.[1 2] We present three patients treated with photodynamic therapy (PDT) for choroidal neovascular membranes (CNVM) who had full-thickness retinal thinning that mimicked an FTMH on OCT.

Case reports

A 58-year-old woman with moderate myopia (−5.00 D) presented after four PDT sessions (spot diameters: 4.4–4.7 mm) for CNVM in the left eye; visual acuity was 20/63. Examination showed subfoveal fibrosis with adjacent atrophy, whereas OCT showed full-thickness thinning overlying an area of increased reflectivity consistent with treated CNVM (fig 1A).

A 53-year-old woman with high myopia (−17.50 D) was treated with PDT twice (spot diameters: 2.9 and 3.1 mm) for CNVM in the right eye. Vision improved from 20/200 to 20/50. Macular examination disclosed atrophy and subfoveal fibrosis, whereas OCT showed full-thickness retinal thinning overlying hyper-reflectivity at the RPE level corresponding to the treated CNVM (fig 1B).

An 89-year-old woman with age-related macular degeneration (AMD) had PDT four times (spot diameters: 4.6–5.3 mm), for CNVM in the right eye. Vision started at 20/100 and stabilised at 20/320 after treatment. Examination showed subretinal fibrosis and atrophy with minimal subretinal haemorrhage, whereas OCT showed almost full-thickness thinning (fig 1C).

For all the three patients, autofluorescence studies with the Heidelberg retina angiograph (Heidelberg Engineering, Germany) showed no autofluorescence signal,[3] and fluorescein angiography showed no discrete areas of hyperfluorescence corresponding to the areas of thinning on OCT.

Comment

These three patients had on their OCT the appearance of a macular hole after PDT for CNVM secondary to myopia or AMD. Although macular holes in high myopia may be difficult to visualise on examination,[4] we do not believe the patients had true macular holes because examination, fluorescein angiography and autofluorescence did not support this diagnosis. In addition, the OCTs lacked findings often seen with FTMH, such as adjacent intraretinal cystic changes, rounding of the retinal edges or subretinal fluid. Simultaneous CNVMs and FTMHs have previously been reported, but these FTMHs had the typical associated findings.[5 6]

The cause of this ''pseudo-macular hole'' appearance is unclear. Retinal thinning on OCT has been described after PDT for CNVM.[7] This FTMH-like configuration has not been reported, but may represent a severe form of post-PDT thinning. However, the ''pseudo-macular hole'' diameters were smaller than the spot diameters used. Parafoveal retinal thinning and geographic atrophy with retinal thinning have been seen on OCT in myopia[8] and AMD,[9] respectively, but not to the degree seen in our patients. The fovea does not appear to be selectively affected; foveal sparing allowed the first two patients to retain relatively good vision.

OCT findings must be interpreted in the context of examination and ancillary test results and not in a vacuum, as this could lead to an erroneous diagnosis of FTMH and recommendation of surgery. Clinicians should be aware that full-thickness thinning mimicking an FTMH may present on OCT in patients with AMD or myopia and a history of PDT.